ABSTRACT OF THE DISCLOSURE

The HIV regulatory proteins Tat and Rev accumulate in nucleoli of human cells. No functional role has been attributed to this localization. Recently it was demonstrated that expression of Rev induces nucleolar re-localization of some nuclear factors involved in Rev export. Thus, it is likely that the nucleolus plays a critical role in Rev-mediated export of singly spliced and unspliced HIV-1 RNAs. As a test for trafficking of HIV-1 RNAs into the nucleolus, a hammerhead ribozyme which specifically cleaves HIV-1 RNA was joined to the U16 snoRNA resulting in accumulation of the ribozyme within nucleoli of human cells. Stably transduced human T-cells expressing this nucleolar localized ribozyme dramatically suppressed HIV-1 replication, confirming a possible trafficking of the HIV RNA through the nucleoli of human cells. In addition, a TAR element which binds Tat was joined to the U16 snoRNA, also resulting in localization in the nucleoli and inhibiting HIV replication.